ABSTRACT

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Nerve agents belong to the group of OFI that irreversibly binds to acetylcholinesterase (AChE). Neurotransmitter acetylcholine (ACh) is not degraded and its increased concentration causes excessive aggravation of cholinergic receptors, known as acute cholinergic crisis [Patočka, 2004].

The main aim of this study was to compare the relationship between structure and inhibitory effect of AChE reactivators. This knowledge can be used in designing structures of new peripherally acting AChE inhibitors with a reversible effect. The mechanism of peripheral inhibition of AChE is already used for prophylaxis of nerve agent poisoning. The mechanism of action is that reversible inhibitor binds to AChE, it prevents binding of nerve agent on this enzyme.

Reversible AChE inhibitors are also used in the treatment of myasthenia gravis and in anesthetic practice, to reverse the action of muscle relaxants administered [Brufani, 1997], where the increased concentration of ACh at the neuromuscular synapses is desirable to restore the physiological function of muscles [Palin, 2002].

Inhibitory potential of AChE reactivators was determined *in vitro*. The inhibitory effect each reactivator was measured by its ability to inhibit every point in the concentration range from 10^{-1} to 10^{-8} mmol/l. Reactivators inhibited enzyme, eel AChE, for 10 min. A buffer with DTNB and ACh was then added. Values of oximolysis were determined to increase the validity of measurement, which were subsequently subtracted from the absorbance values to avoid reading false-positive results.

An increase of the inhibitory potential of AChE reactivators with bisquaternary oximes groups in the *ortho* position was found, in comparison with other positions on the pyridine nucleus. Simultaneously, the higher inhibitory potential was also demonstrated bisquaternary oximes with longer connecting chain (10 carbons). Also, substitution on the coupling chain increased the inhibitory potential against AChE.